(1)

TRANSLATION NO. 227

DATE: July 1968

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

11 227

Q Fever.

by E. N. Bartoshievich (Alma-Ata) of the Institute of Krai Pathology of the Academy of Sciences of the Kazakh SSR.

Klinicheskaia Meditsina. 35: 2: 137-141: 1957.

In 1946, in the journal "Klinicheskaia Meditsina", No 6, in the article "Short Epidemic Diseases of an Undetermined Etiology," we informed of the various acute, feverish, benign diseases which are observed yearly in the spring and summer among the inhabitants of Alma-Ata and the surrounding Rayons of the Alma-Ata Oblast. With the assistance of careful bacteriological and repeated serological investigations and also intracutaneous allergy tests and epidemiological data, we eliminated the possibility of these diseases belonging to the typho-paratyphous group, exanthematous fever, brucellosis, tularemia, influenza and the leptospiroses. We assume that the described diseases are a new disease entity to the USSR distinguished from all other investigated infections. After the establishment of Q fever in Uzbekistan by A. I. Shifrin, the true nature of the spring-summer epedemic diseases in Alma-Ata Oblast was revealed. They also proved to be Q fever.

Starting with 1954, we conducted work on the serological diagnostics of Q fever. We studied the reaction of the fixation of the complement with the antigen Rick. burneti (the live strains, "Termez" and "Konstantsiia") not only in the patients who had recovered or were recovering in the clinic in past or present years, but also in the persons who were subject to this disease in the past and were released from the clinic with the diagnosis, "short febrile disease of unknown etiology". We were able to retrospectively confirm a diagnosis of Q fever in 144 patients who had become ill with this infection from 2 to 8 years before. What attracts the attention is, the protracted retention of the complement fixing antibodies to Rick. burneti in the serum in a titer of 1:5-1:160, whereupon the titer and the intensity of the reaction diminish in proportion to the time lapse after recovery from the disease.

By our observations, in the endemic areas, isolated sporadic cases of Q fever may be encountered during the whole year; with the advent of dry warm days, the number of patients is sharply increased, reaching the maximum figures in May-June. Beginning with July, the number of sicknesses noticeably decreases, in September they are seldom observed.

From the aggregate number of 195 patients, 149 patients (76 %) were city residents, and during the course of last year did not leave the limits of the city. 21 were also city residents, but shortly prior to the disease (for 10-23 days) were on missions in the Rayons of Alma-Ata Oblast or in other Oblasts. 25 patients were residents of collective farms near the city. We were able to establish that there had been direct contact with domestic animals in only 63 patients (32 %).

It is known that the pathogen of Q fever (Rick. burneti), reaching an exterior environment with the excretions of domestic animals, can sustain it-

self in a dried condition and be spread with the dust even beyond the limits of an endemic nidus (M. P. Chumakov and Ia. P. Beliaeva, 1954; I. A. Shifrin, 1954; S. M. Kulagin and R. I. Zubkova, 1955; and others). It is possible that the dust factor, i.e., the aerogenic (it is felt by the translator that this word should read "air-borne") path of the infection has a basic importance in the spring-summer seasonableness of Q fever in Alma-Ata. The espressed hypothesis is confirmed in the overwhelming majority of those who became ill (68 %) by the absence of contact with domestic animals and also their products. There is also noted a great intensiveness of the diseases in connection with dry and warm weather (much dust).

In 1955, for the clarification of the sources of infection in an endemic Rayon, we investigated 845 head of large, harned cattle. In 33 % of them we noted a positive reaction of the fixation of the complement with the antigen Rick. burneti in a titer of 1:10 (the serum was not titrated higher in order to spare the antigen). The demonstrated intensity of the reaction after 24 hours (+ + + + and + + +) gives the basis to consider that the reaction would have been positive even at higher titers. The animals which we investigated belonged to various collective farms situated around Alma-Ata (Iliiskii and Kaskelenskii Rayons), and also branch industries of separate establishments. The infectivity of the large horned cattle in the various collective farms and industries ranged from 14 to 62 %. In the number of animals under investigation were privately owned cows belonging to residents of Alma-Ata (12), and to collective farmers of 'kolkhozes' near the city (203). Among these, the animalswhich were infected proved to be an even 40 %, and this milk is actually used, mainly by the inhabitants of Alma-Ata.

Our work in this direction has only started. The next in line is the investigation of the small, horned cattle, horses and dogs in relation to the intensiveness of the spread of the infection among them. Q fever is not transmitted from person to person. In many years of studying this infection, we have not once witnessed intrahospital infections. Nidal infections are encountered, but they, as a rule, are connected with the use of milk from the same cow, or with some other type of contact with animals. This year, we twice observed nidi of the disease. In one case three members of a family became ill almostsimultaneously, the family had been using unprocessed milk from their own cow which had just calved; and in the other analogous case, two members of a family became ill. We did not observe large outbreaks among the population of one Rayon, ward,or area, one should only note that the persons who become ill more frequently are those living not in the center of the city, but in the wards where there are many private homes and individually owned cows.

The clinical picture of Q fever in the 195 patients with the serologically confirmed diagnosis (the reaction of the fixation of the complement with the live antigens of Rickettsia burneti, of the strains "Termez" and Konstantsiia", in a titer from 1:20 to 1:640, no weaker than + + +) almost completely corresponds to the clinic described by us in "Short Endemic Diseases of an Unexplained Etiology," and also to the clinical picture of Q fever in the territory of the Central Asian Republics and in other areas of the Soviet Union (A. I. Shifrin, 1953, 1954; M. P. Chumakov and A. P beliaeva, 1954; M. P. Chumakov, A. P. Beliaeva, A. I. Shifrin, N. I. Khodukin and V. A. Lysunkina,

1954; G. S. Pul'pinskii, 1954; S. M. Kulagin and N. K. Kokcheeva, 1954; B. Kh. Burganskii, 1954; V. A. Lysunkina and N. L. Mosharovskaia, 1955; P. F. Zdrodovskii, 1955; and others).

The disease began acutely in the overwhelming majority of the cases (in 68 %). While enjoying complete health, there suddenly occurred a rigor causing shock (in 32 %); the temperature in the course of one or two days rose to high figures - 39-40°. The patients complained of strong headaches (which, by our observations, together with a high temperature constitutes the first symptom of the disease), a general weakness, a sensation of breakdown, aches in the muscles of the entire body (in 80 %), at times localized pains in the gastrocnemius muscles(in 49 %), in the loin (in 47 %) and less frequently in the bones and joints (in 9 %) without objective changes in regards to the latter. In many of the patients the following were observed: hyperemia of the face (in 49 %) and injection of the sclera (in 53 %) at times sharply expressed; occasionally pains in the eyeballs (in 10 %); significantly less frequent-dizziness (in 3 %); vomiting, not connected with eating (in 6 %); nausea (in 6 %); and in single cases, nosebleeds. Also, the disease sometimes took a course with repeated small chills prior to the evening raise of the temperature (in 11 %). Significantly less frequently, the disease began gradually (in 32 % of the patients) with a general malaise, weakness, a sensation of breakdown, headache and an increase of the temperature (to 38°); such patients during the first 2-5 days usually continue to work and do not consult a doctor.

As a rule, the appetite decreased after the first days of the disease (in 90 % of the patients); the tongue was covered by a white film.(in 72 %) and in the majority of the patients remained moist (in 82 %), often with impressions of the teeth around the edges (in 47 %). The abdomen was usually soft, not swollen, sometimes a rumbling was noticed in the ileo-caecal region (in 26 %). The stool was most frequently normal (in 72 %); constipation was less frequently observed (in 25 %); and as an exception (in 3 %), there were fluxes of an entiric nature 2 or 3 times a day, this passed without treatment. Now and then patients complained of pains in the epigastric region (in 3 %), and in 3 patients we observed diffuse pains along the entire abdomen, whereupon one of these patients was suspected of having appendicitis and sent to the surgical clinic where the diagnosis was not substantiated. After the 4-6th day of the disease, in the majority of the patients (in 60 %), the liver and less frequently the spleen palpated (in 44 %), but towards the end of the febrile period, with the patient on his side, the spleen was detected almost as often as the liver (in 62 % of the patients).

Expressed catarrahs of the upper respiratory tracts are not natural for Q fever and are very rarely observed. Thus, hyperemia of the pharynx was observed in only a few of the patients (in 9.5 %), rhinitis and tussiculation (in 20 %). In the majority of the patients (59 %), at the climax of the disease, bronchitises were detected; pneumonias, according to our data, are seldom encountered. We should point out that we paid special attention to the condition of the lungs, and in addition to a careful daily auscultation, we subjected each patient to a mandatory roentgenoscopic investigation at the climax of the disease (on the second day after admittance) and sometimes follow-up investigations at the end of the febrile period. However, regardless of such a directed investigation of the lungs, pneumonia could be es-

tablished in only 24 patients, 14 of them- clinically and roentgenoscopically, and in 10 - by roentgenoscope alone. In the 14 patients the pneumonia was of a focal type with the localisation of the inflammatory process on the narrow section in one of the lower lobes of the lung and was characterized by meager clinical symptoms. In the 10 patients we noted with the roentgenoscope only an amplification of the pulmonary pattern in the radical zone of one of the lungs (in the lower lobe in one of the patients) which passed without a trace upon recovery. Of the 14 patients with the clinically established pneumonia, four complained of a pain in the thorax which corresponded to the localisation of the inflammation; 10 patients had a dry cough.

V. A. Lyashkina and E. L. Kozlovskaia (1955) informs that pneumonias with Q fever occur late, after the temperature has already lowered, and it is only possible to distinguish them by repeated roentgenoscopy. In this manner the authors succeeded in diagnosing pneumonia in 14 of 19 Q fever patients. In the period of convalescence, after the establishment of a normal temperature, we carried out a control roentgenoscopy in 28 patients, but changes that are characteristic for pneumonia were not observed.

The cardiovascular system in Q fever suffered little with the exception of a marked bradycardia (in 77 % of the patients). In some of the patients of an older age (11 %) we observed an insignificant dullness of the heart sound, without a dilatation of the heart outlines, and an infrequent lowering of the maximum arterial pressure (in 4 %). In all the other patients the arterial pressure was normal.

Regardless of the high temperature and strong headache, the consciousness of the patients was completely preserved, insomnia was sometimes noted (in 16 %). We observed a marked typhous condition in only one patient; night time delirium (in 5%) and meningitic phenomena (in one patient) were infrequently noted.

In the majority of the patients the skin of the body was dry and became moist only upon the lowering of the temperature; in the other patients a heavy sweating was observed throughout the entire course of the disease (16%). In foreign as well as in Soviet literature it is emphasized that exanthema is not characteristic for this species of rickettsiosis. Our observations also substantiate this. Never the less, in some patients eruptions can appear even with this infection. We observed in 8 patients* a polymorphic rose rash at the climax of the disease (on the 4-9th day). The eruptions were usually sparse and in a form of isolated elements located on the skin of the front planes of the thorax and abdomen, less frequently on the dorsum, and extremities (more often on the upper extremities). The sizes of the separate elements of the rash ranged from 2-3 to 4-6 mm, in six patients they were of a rose speckled form and in two patients they raised above the skin level, disappeared during the febrile state and again appeared. The rash, as a general rule, lasted from 2 to 5 days, not leaving a pigmentation. In two patients we observed an herpetic rash on the wings of the nose and lips.

A remittant temperature is characteristic for Q fever (in 77% of the patients), less frequent is a temperature of a persistent type (in 23 %). The temperature remained at high figures an average of 6-10 days (in 60 %),

but the disease sometimes even took an abortive course - 2-4 Days (in 5 %), and was protracted to 2 weeks (in 12 %) and less frequently to 3-5 weeks (in 13 %). Analyzing the temperature curves, one should note the clear undulation in some of the patients (in 7 %), particularly with the prolonged course of the disease (3-5 weeks) and the relapses (in 9 %). The relapses occur after 1-5 days of a normal temperature, are of short duration, and do not particularly reflect the general condition of the patients.

Not once did we observe complications or lethal results. The convalescent period passed smoothly and the patients, after 2-3 days of a normal temperature, usually asked to be sent home. For the past two years, while retrospectively and serologically perfecting the Q fever data on those patients who were discharged from the clinic, we completely unexpectedly discovered that several of those who had been released from the clinic in good condition were again on the hospital's records. They were unable to work due to a great weakness. Now we discharge patients who have recovered from Q fever no earlier than the 5-7th day of a normal temperature, individualising in each separate case the length of leave and the return to work.

In regards to the erythrocytes, one will not notice observable changes. Changes of the leukocytes are expressed sufficiently sharply, but they are variegated (evidently in the strength of the individual reactions of the macroorganism) and therefore are difficult to yield to a generalization. In the majority of the patients (in 55 %) the quantity of leukocytes remained normal (whereupon it was more often on the lower limitation of the norm than on the upper), leukopenia was a little less frequently observed (in 40 %) sometimes acutely expressed (below 3,000 in 30 % of the patients) and very seldom, a mild leukocytosis (in 5 %). Independent from the quantity of leukocytes, in the leukocytic formula a displacement of a various degree to the left is noted, sometimes as far as the mielocytes, whereupon, in the majority of the patients, a normal quantity of neutrophils was preserved (in 52 %), less frequently with neutrophilia (in 18 %); 30 % of the patients had neutropenia with a comparative lymphocytosis. In 50 % of the patients the eosinophils were preserved in the peripheral blood, histiocytes (from 1 to 10) and Turk's cells (in 50 % - from 1 to 4) appeared in 77 % of the patients. The blood of all patients was checked for sterility and for an agglutination reaction with typho-paratyphous antigens, brucella, Proteus X_{19}, leptospirae and tularemia antigens with a negative result.

In order to economize on the antigen, we conducted single-stage serological investigations for Q fever in the majority of the patients during the convalescent period prior to the discharge of the patients from the clinic, usually between the 14th and 21st day of the disease. We arranged the reaction of the fixation of the complement with live Rick. burneti (the strains "Termez" or "Konstantsiia") in a titer of 1:5, 1:10, 1:20, 1:40, less frequently 1:80 and higher. We considered as positive a reaction with its intensity no weaker than + + + after 24 hours. As a rule every arrangement of the reaction was accompanied by appropriate controls. As a standard Q fever serum we used the serum of our own patients who had a titer of no less than 1:320-1:640. A clear positive result (from 1:20 to 1.80) was received in all our patients, whereupon in 31 patients there was noted an increase of the titer in dynamics (1:20-1:40 to 1:160-1:640). As indicated above, in order to spare

the antigen we usually made no large dilutions of the serums (to 1:40), and only in a few patients that were of special interest for us (those with rashes, pneumonias, prolonged fevers) did we start an investigation from the 8-10th day of the disease and after that traced the increase of the complement fixing antibodies dynamically.

By our data, the complement fixing antibodies in some of the patients appear in the blood serum from the 7-10th day (1:5, 1:10, infrequently 1:20), but the intensity of the reaction will not be great and on the following day will usually drop from ++++ or +++ to ++ or even +, growing more intense in the following days. From the 14th-18th day of the disease, the complement-fixation reaction will come out positive in 85 % of the patients in a titer 1:20-1:40 (++++) and the intensity of the reaction gives the right to assume a higher titer of the antibodies. In the fourth week of the disease the complement-fixation reaction came out positive in all of the patients checked (41 patients).

The complement fixation reaction with Q fever patients is a very clear and sensitive reaction, increasing dynamically for the duration of the disease or, conversely, declining in titer and intensity if the patient had undergone this infection in the past (anamnestic reaction).

Synthomycin and levomycetin are of little effect in Q fever, biomycin checks the temperature on the 2nd or third day after taking taking the preparation.

Footnote

*- All 8 patients were dynamically tested for other forms of rickettsioses with the specific antigens with a negative result.